IND Cumulative Table of Contents (CTOC) Review Demonstration Participation

Purpose:

This demonstration is designed to provide demonstration electronic INDs using CTOC to the Agency. This will help us gain experience with using XML based systems in the review process using more realistic data than is otherwise available. The files described here may or may not be similar to the file submission standards being developed within the International Conference on Harmonization (ICH) Common Technical Document (CTD) in the M2 group.

The technical approach for an electronic CTD (eCTD) being developed by the M2 includes specifications for the file formats for documents and data as well as metadata about the submission. The submission metadata provides information about the submission that can be used in applications developed by the regulatory agencies. An XML DTD is being developed to transport the submission metadata. It may be different than what is described here.

More information regarding the CTOC project is available at the following web site:

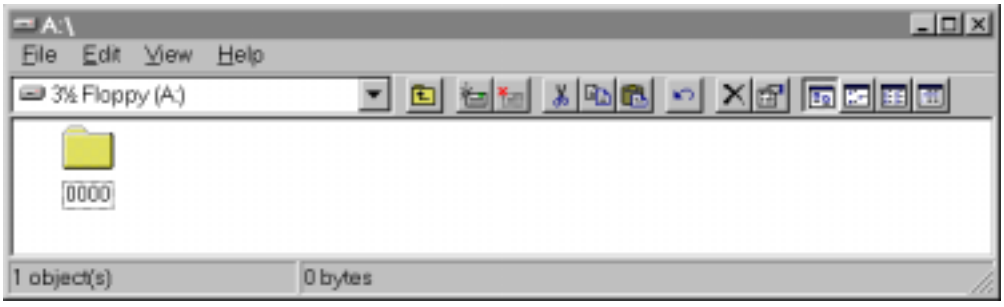
http://www.fda.gov/cder/regulatory/ersr/ctoc/default

Organization of Files:

Place all the files that are to be included with your demonstration into a single folder that is named with a four digit number representing the serial number of the submission. For example, the files for the first submission should be place in a folder named “0000” and the files for the second submission should be in a folder named “0001” and so-on.

Subfolders:

There is no specified organization of files other than placing them in the folder described in the previous paragraph. You may choose to create subfolders within the serial numbered folder and this is acceptable (as long as the links created in the CTOC files are correct). For example the folder containing the files for the first submission to an IND is numbered 0000 and looks like the following picture:



CTOC files:

Each serial numbered folder has its own admin.xml file and a Table of Contents (TOC) file for each module that is affected by the submission and the files containing information for review. There are five modules and they are based on the International Conference on Harmonization (ICH) Common Technical Document (CTD) modules. The admin.xml file points to the latest submission of a module's TOC file. For example, if both folders "0000" and "0001" have clinical module TOC files, the admin.xml file points only to the one in folder "0001". That is because the module TOC file in folder "0001" will contain all the file references in the earlier module TOC file with the new file references. The filenames for module TOC files are not specified, but they should have "xml" as their filename extension.

The CTOC files can be prepared in a number of ways. If you wish to use the author tool that was used to produce the working model presented by the agency, the setup for it is in this zip file extraction. You will find it in the subfolder named TOCeditor. There is a file named Read_Me_TOCeditor.pdf that you should read before you setup the tool.

If you wish to create the CTOC files using another method, please see the file named " XML Specification" in the subfolder named "Documentation" that was created with this zip file extraction. It describes each component of the CTOC files and their purpose.

Document Type Definitions (DTDs)

CTOC uses DTDs that are separate from the CTOC files. Within each CTOC file, on one of the top 3 lines, is a declaration that provides the filename and path for the DTD controlling the format of the file.

The CTOC files should validated according to the Document Type Definitions before submission to the Agency. There are a number of ways to do this. One of the ways is to use the document reference validation tool described in the next section. If you wish to use some other method, a description of each DTD follows:

The admin.xml file is defined by the "admin_v500.dtd" DTD file. The module TOC files are defined by the "ctoc_v500.dtd" DTD file. These DTDs are available in the CTOC Model Download available at the web site referenced above or in the subfolder named "CTOC Model Download" that is part of this zip file extraction. If you follow the instructions included with the download, you can find the DTDs at the following filename and path:

[drive]:\CTOC_Demo\Resource\CTOC\admin_v500.dtd
and
[drive]:\CTOC_Demo\Resource\CTOC\ctoc_v500.dtd

The "ctoc_v500.dtd" DTD file will refer to two lists, one for category values and one for subcategory values. These are also DTD files and are available in the working model download at the following path and filenames:

[drive]:\CTOC_Demo\Resource\Common\category_v500.dtd
and
[drive]:\CTOC_Demo\Resource\Common\subcategory_v500.dtd

The DTD documents are also available by hyperlink from the following page:

http://www.fda.gov/CDER/REGULATORY/ERSR/CTOC/Default.htm

Validation of CTOC Document References:

The CTOC document references and related document references can be confirmed in a number of ways. This can be done using the validation software available in the subfolder named "Validation Tool" that is part of this zip file extraction.

The Read_Me_Validation.pdf file that is in the download describes how to use this tool.

Testing the Submission: (Requires Microsoft Internet Explorer 5.0 (IE5) or higher)

There are two ways to test the submission, you can use a copy of the resource folder locally (Local Resources) or you can reference the internet resources (Remote Resources).

Local Resources Testing:

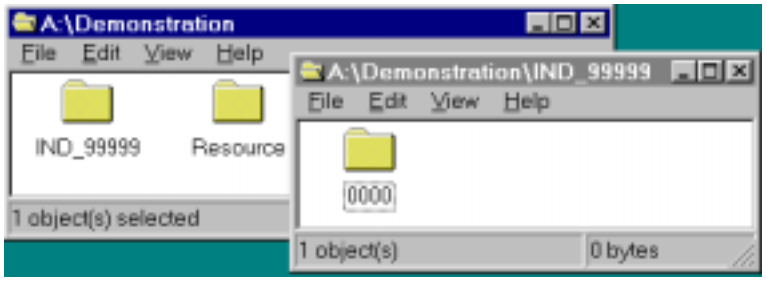
To test the submission with local resources you will need a copy of the "Resource" folder with its subfolder and file contents. This is available from the "CTOC_Demo" at the following path:

[drive]:\CTOC_Demo\Resources\

Complete the following steps:

1. Create a folder to hold your CTOC demonstration and name it "Demonstration"
2. Place a copy of the "Resource" folder with its subfolders in the "Demonstration" folder
3. Create a subfolder within the "Demonstration" folder and name it "IND_99999"
4. Place your serial numbered submission folder (from the "Organization of Files section above) within this "IND_99999" folder.

When you are finished the folders should appear as they do in the picture below:



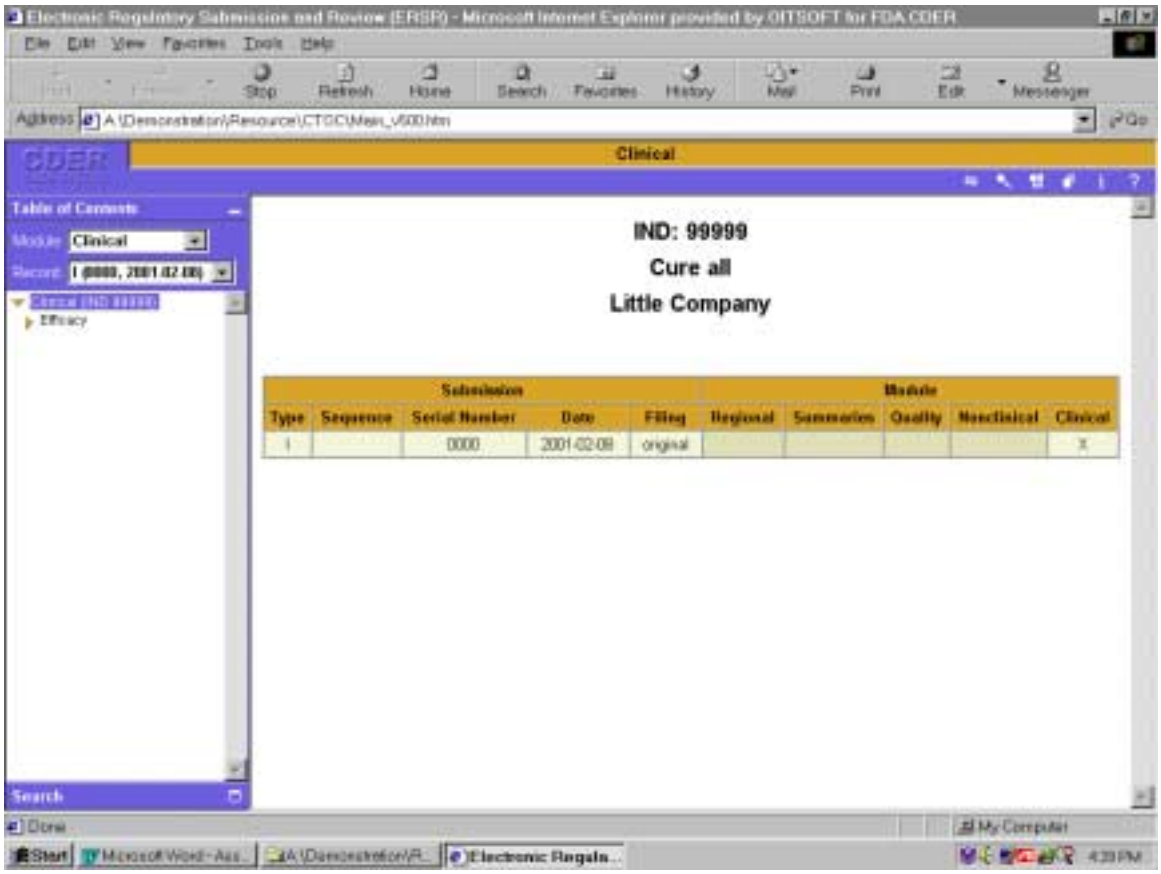
Run or open the file with the following filename path:

[drive]:\Demonstration\Resource\tool\Main_v500.htm

IE5 will prompt you for the location of the admin.xml file for the submission you wish to test. Type the directory path (not the filename) for the admin.xml file. For example, in this case it would be the following:

[drive]:\Demonstration\IND_99999\0000\

If you followed the CTOC example in the Read_Me_Author_Tool.pdf document (available in the TOCeditor subfolder) you should get something like the following picture on your screen:



This will function the same as the CTOC_Demo download

If you want to test more than a single demonstration submission to the same IND you should place each submission folder within the IND_99999 folder. When prompted for the location of the admin.xml file you should provide the location of the most recent (highest serial number) admin.xml file.

Remote Resources Testing:

Remote resources testing requires an internet connection.

The Resource Declarations in the admin.xml file and in the TOC files should provide the internet path for each of the four files being referenced.

The resource declarations occur as the second and third line of each CTOC file. The internet path for each resource file is provided below:

admin.xml
http://www.fda.gov/cder/regulatory/ersr/ctoc/resource/CTOC/admin_v500.dtd
http://www.fda.gov/cder/regulatory/ersr/ctoc/Resource/ctoc/admin_v500.xsl

Module TOC files
http://www.fda.gov/CDER/REGULATORY/ERSR/CTOC/Resource/CTOC/ctoc_v500.dtd
http://www.fda.gov/CDER/REGULATORY/ERSR/CTOC/Resource/CTOC/ctoc_v500.xsl

The CTOC files in the demonstration submission should use these internet paths in their declarations when they are submitted to the Agency.

To test the CTOC Demonstration submission using remote resources, address the following file using your IE5 browser:

[drive]:\Demonstration\resource/tool\Main_v500.htm

You will be prompted for the path to the admin.xml file for the submission you wish to test. Using the same file structure as described in the local resources testing you should get the same result.

Send it to Jon:

Once you are finished with the "Remote Resource Testing" contact Jon Clark at CLARKJO@cder.fda.gov. You will be asked to send your demonstration to him either on disk or by e-mail (depending on the nature of your submission).

If you are having trouble, don't hesitate to contact Jon Clark.

Your demonstration will be tested and will be placed in a secure location where our reviewers can access and make comments about it. You will receive feedback from Jon regarding your demonstration and a non-proprietary summary of how it compares with others.

It would be of the most value if these demonstrations could be received and evaluated before the May, 2001, ICH meeting.